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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,580	08/20/2001	Sandor Szalma	MOLESIM.025A	5589

20995 7590 09/09/2003

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

7

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,580	SZALMA ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 1-12 and 17-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Applicant's election of Group V, claims 13-16 is acknowledged. This application contains claims 1-12 and 17-19 drawn to an invention nonelected without traverse in Paper No.

6. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-19 are currently pending.

An action on the merits of elected claims 13-16 follows.

Abstract Objection

The abstract of the disclosure recites "a system and methods for rapidly accurately assessing ligand binding characteristics for diverse classes of protein molecules." This is an incomplete sentence and requires correction.

Oath/Declaration

Please submit a new copy of the declaration as the date and the country of citizenship for Lisa Yan is illegible.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The method of claims 13-15 for identifying a target protein comprising selecting a target, retrieving a fingerprint, and comparing a fingerprint is merely a mathematical manipulation of data. The apparent series of mathematical steps for the data manipulation is equivalent to a mental process. Applicant is reminded that mental processes are not statutory subject matter under 35 USC 101.

The claimed subject matter is not restricted to be a computer-implemented method, however the specification indicates that these processes are to be done on a computer using software known in the art. In the event that the claimed method steps are implemented by a computer, the method steps are not statutory as any computer implemented method must produce a result which is concrete, tangible, and useful (MPEP 2106.IV.B).

Claim 16 is directed to a system comprising a database and an engine to run a method similar to claim 13. Claim 16 does not recite any structural limitations.

“The mere fact that a hardware element is recited in a claim does not necessarily limit the claim to a specific machine or manufacture.” See also *In re Iwahashi*, 888.F.2d 1370, 1374-75, 12 USPQ 2d 1908, 1911-12 (Fed. Cir. 1989), recited with approval in *Alappat*, 33 F.3d at 1544 n.24, 31 USPQ2d at 1558.

It is noted that a claim may be statutory when it identifies the physical structure of an item of manufacture in terms of its hardware, or a hardware and software combination. Claim 16 does not recite any physical or hardware limitations, as set forth above. It is also noted that a claim to a product which has a practical application in the arts may be statutory; e.g. a computer comprising a program which produces a concrete, tangible, and useful result, as decided in *Alappat* (312 USPQ2d 1557) and *State Street* (47 USPQ2d 1601). As set forth above, the claimed method does not produce a concrete, tangible, and useful result, therefore the computer readable medium comprising a program for running such a method would not have a practical application in the arts, and is not statutory.

Claims 13-16 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claims 13-16 are directed to a method of identifying a target protein for pharmaceutical intervention and a system for biological research. However it is not clear what result is produced by the said method or system. The “usefulness” of identifying a target protein by the recited steps is not apparent, as there is no step of identifying a protein and the fingerprint generation and comparison “usefulness” is not clear, as the specification teaches that the invention can be used to create functional associations between a first and second protein without stating the

Art Unit: 1631

usefulness of doing such a comparison (page 3). The specification goes on the state that protein/ligand interactions can be calculated and the nature of the interaction identified as a fingerprint. Further, the fingerprint may be used to identify similarities between various proteins (page 8). However, the usefulness of this fingerprint as it relates to identifying a target protein remains unclear. It is noted that in order for this method to be useful for these purposes, other information is required, such as identification of an actual target protein by following detailed steps that utilize specific parameters to perform the method. Utilities that carry out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities (See MPEP 2107.01). Further, as set forth in *Brenner v. Mason* (148 USPQ 689 (1966)) and *In re Ziegler* (26 USPQ2d 1600), the "usefulness" of an invention must be immediately apparent to those familiar with the technological field of the invention. As further research, mathematical calculations, and method steps would be required to "use" the instant method and system the apparent result of the method and system is not "immediately useful" and lacks utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or

Art Unit: 1631

absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to select a target protein and retrieve a fingerprint to compare with other generated fingerprints for proteins that represent the entire human genome. For the reasons discussed below, this constitutes undue experimentation.

b) and d) The specification provides no direction on how to select a potential target protein. Further, the specification is devoid of information on exactly what steps to take to generate a fingerprint such that the fingerprint may be compared and contrasted to another fingerprint from a different protein. A fingerprint apparently is a set of values representative of the binding strengths of the different proteins, however, there is no guidance on the parameters for obtaining such information. In pharmacophore analysis and lead generation, it is known that various descriptors are utilized to characterize molecules. However, the instant specification provides no exact details on just what the fingerprint values consist of and how they are generated. The specification states that the "protein/ligand interaction comparisons comprise identifying the nature of the ligand interaction with each protein in the comparison. Typically the protein/ligand interaction is characterized by a bonding affinity between each protein and each ligand. This could be binary or it could be a numerical variable, such as an equilibrium binding constant or a binding energy (page 7, beginning line20)". Without guidance on the specific generation of the binding constant or the binding energy or perhaps some other variable that would represent a fingerprint, the present invention is not enabled.

c) The specification provides no working examples of the said method.

e) and g) It would have been well known in the art that descriptors function to characterize molecules so that they may be compared to identify potential drug candidates. The research in this field is quite extensive and there are several computational programs that implement comparisons of descriptors in order to characterize biological activity. However, absent the guidance on how exactly to perform the broad steps of this invention, one of skill in

Art Unit: 1631

the art would not have sufficient teaching in order to retrieve and interaction fingerprint and compare it with another for the several thousand proteins in the human genome.

The prior art, for instance, teaches that methods to describe the similarities of molecules have gained increasing interest in rational drug design. Beyond database searching there are many applications of similarity metrics. There are numerous ways to assess the similarity of molecules, **depending on the choice of molecular properties** to compare (Briem et al. J. Med. Chem. (1996) Vol. 39, pages 3401-3408). Briem et al. go on to describe their particular method to compare molecules, known as a DOCK-generated fingerprint method. As is quite clear in this method, the steps are detailed in terms of the generation of the fingerprints and similarity indices (see page 3402 and 3403 formulas). However, the instant specification does not provide the details in such a way that one of skill in the art would know what formulas to use, what databases to use, how to fit them together or distinguish them from any other protein comparison method that exists in the prior art. The generic nature of the specification does not enable one to practice the methods steps of the instant claims.

f) The skill of those in the art of bioinformatics and pharmacogenomics is high.

h) The claims are broad because they are drawn to a method of generating a fingerprint with no further instructions. The skilled practitioner would first turn to the instant specification for guidance to practice methods of generating fingerprints. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance however the prior art shows that there are numerous methods based upon protein interactions.

For the reasons set forth above it would require undue experimentation for one of skill in the art to practice the claimed invention therefore the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1631

Claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites a "method of identifying a target protein for pharmaceutical intervention comprising (a) selecting...(b) retrieving...(c) retrieving...(d) comparing...and (e) repeating". Nowhere in the instant claim is there a step of identifying a target protein. It is unclear what method applicant actually intends.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.


MARJORIE MORAN
PATENT EXAMINER

September 5, 2003
Lori A. Clow, Ph.D.
Art Unit 1631

